Articles

Tremor Disorders
Diagnosis and Management

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Tremor is commonly encountered in medical practice, but can be difficult to diagnose and manage. It is an involuntary rhythmic oscillation of a body part produced by reciprocally innervated antagonist muscles. Tremors vary in frequency and amplitude and are influenced by physiologic and psychological factors and drugs. Categorization is based on position, posture, and the movement necessary to elicit the tremor. A resting tremor occurs when the body part is in repose. A postural tremor occurs with maintained posture and kinetic tremor with movement. Various pathologic conditions are associated with tremors. Essential tremor, which is the most common, is postural and kinetic, with a frequency between 4 and 8 Hz, and involves mainly the upper extremities and head. Essential tremor responds to treatment with primidone, β-blockers, and benzodiazepines. Parkinson's disease causes a 4- to 6-Hz resting tremor in the arms and legs that responds to the use of anticholinergics and a combination of carbidopa and levodopa. Tremor can also be a manifestation of Wilson's disease, lesions of the cerebellum and midbrain, peripheral neuropathy, trauma, alcohol, and conversion disorders. Treatment should be directed to the underlying condition. Stereotactic thalamotomy or thalamic stimulation is a last resort.

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Tremor is an involuntary, rhythmic, oscillatory movement produced by reciprocally innervated antagonist muscles. It is commonly seen in general medical practice, and the diagnosis can be challenging to clinicians. Therapy for the many types of tremor depends on making the correct diagnosis. We review the different categories of tremor, their clinical presentation, and current treatment modalities.

Classification

There are two classification systems used in evaluating tremor.[1] The first is based on whether tremor occurs at rest (resting tremor) or with action (Table 1). Tremors with movement (action) are subdivided into postural tremor, which occurs with maintained posture; kinetic or intention tremor, which occurs with movement from point to point; and task-specific tremor, occurring only when doing highly skilled activity. A postural tremor is tested by having a patient hold the arms stretched out in front. Kinetic or intention tremor is tested by the finger-to-nose maneuver.

The second tremor classification is by cause. Tremor can be due to a variety of conditions, both physiologic and pathologic (Tables 2, 3, and 4).

Physiologic Tremor

Physiologic tremor occurs normally when attempting to maintain posture. The frequency is 8 to 12 Hz in the hands, but may be as slow as 6.5 Hz in other body parts.[2] The frequency decreases with age, especially after the fifth decade. Under certain circumstances and with drugs, it can increase and become symptomatic (Table 2). Conditions such as emotional stress and exercise can enhance physiologic tremor. Drugs such as amphetamines, certain anticonvulsants, and antidepressants also may exacerbate the tremor (Table 3). The best therapy is to remove the cause, but if that is not possible, then trying a β-adrenergic antagonist such as propranolol hydrochloride might be helpful.

Tremor can occur in a variety of pathologic conditions (Table 4). The more common ones will be discussed.

Essential Tremor

Essential tremor is the most common movement disorder. It is estimated to affect in excess of 1 million persons in the United States.[3] There is no sex or racial difference, and it often occurs in families as an autosomal dominant trait. Its onset is insidious with varying progression over time. It may appear in childhood or adult

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TABLE 1.—*Tremor Classification*

Tremor Type	*Occurrence*
Resting	When limb is fully supported against gravity and the muscles are not voluntarily activated
Postural	When limb is positioned against gravity
Kinetic	During any type of movement
Intention	Exacerbated toward the end of goal-directed movement
Task-specific	Only during performance of highly skilled activities such as writing or playing music

life, and it slowly progresses with age. The frequency is usually between 4 and 8 Hz. It is most evident with hands held in posture and attenuates during voluntary movement. In some patients, however, the tremor is most severe with movement. At times, when severe, it may persist at rest, making the distinction from Parkinson's disease difficult.

The hands are most affected, but other body parts may also be involved. Head tremor, commonly associated with hand tremor, may occur in isolation and may show a different pharmacologic response from hand tremor. Speech involvement (voice tremor) can result from tremor of the muscles of phonation or respiration or of the head and neck.

Variants of essential tremor include primary writing tremor, in which writing elicits a pronation-supination tremor not seen in other arm movements, and orthostatic tremor, which is present in the lower limbs during standing and may disappear with sitting or walking.[3,4] Essential tremor may be associated with other movement disorders, including cervical dystonia, writer's cramp, and spasmodic dysphonia.[5,6]

Although a postural tremor similar to essential tremor occurs in Parkinson's disease, patients with this tremor are not predisposed to Parkinson's disease.[7] Essential tremor lessens temporarily with the ingestion of alcohol, an effect that lasts from 30 minutes to several hours and is an important distinguishing feature. A number of external factors such as emotion and stress exacerbate the severity of essential tremor. Although this condition does not shorten the life span, quality of life may be greatly affected.

TABLE 2.—*Factors That Exacerbate Physiologic Tremor*

Emotions—anxiety, stress, fear
Exercise, fatigue
Alcohol withdrawal
Hypoglycemia
Thyrotoxicosis
Pheochromocytoma
Drugs

TABLE 3.—*Drugs That Exacerbate or Induce Tremor*

Drug Class	*Examples*
β-Adrenergic agonists	Theophylline Metaproterenol sulfate Terbutaline sulfate
Amphetamines	
Anticonvulsants	Valproate sodium
Lithium carbonate	
Neuroleptics	
Tricyclic antidepressants	
Methylxanthine	Caffeine Theophylline
Dopamine agonists	
Heavy metals	Mercury (hatter's shakes) Lead Arsenic
Alcohol	

Treatment

Medical treatment may not be necessary when essential tremor causes no disability. β-Adrenergic–receptor antagonists are the drugs of first choice. Propranolol hydrochloride in daily doses of 80 to 320 mg is given most often.[3] Long-acting propranolol is also effective.

Metoprolol, because of its cardioselectivity, is useful when asthma is present. Nadolol can be effective and has fewer central nervous system side effects.[2] Primidone, an anticonvulsant, has shown a degree of therapeutic response comparable to that of propranolol.[8] In doses of 50 to 250 mg at nighttime, it can markedly reduce tremor. About 20% of patients have an acute idiosyncratic reaction in the form of dizziness, headache, ataxia, nausea, and vomiting.[9] This reaction typically resolves in two to three days and is not a reason to discontinue the medication. The drug regimen should be commenced in small doses, and the patient should be warned of this possible side effect. If the tremor is not controlled with one drug, a combination of primidone and propranolol can be helpful. If tremor is severely disabling and unresponsive to drugs, stereotactic thalamotomy or thalamic stimulation should be considered.[10,11] Sedatives and tranquilizers are rarely effective, although some patients may respond to the use of alprazolam. Clonazepam is, however, the drug of choice in orthostatic tremor.

Tremor of Parkinson's Disease

Parkinson's disease has the symptom complex of tremor, rigidity, bradykinesia, and postural instability. Histologically, there is degeneration of the substantia nigra, and Lewy bodies are present.

Parkinson's disease is neurochemically defined by a dopamine deficiency in the striatum.[9,12] Approximately half of patients with Parkinson's disease present with

TABLE 4.—*Causes of Pathologic Tremor*

- Parkinson's disease
- Other parkinsonian syndromes
- Wilson's disease
- Essential tremor
- Peripheral neuropathy
  - Charcot-Marie-Tooth disease
  - Other hereditary sensorimotor neuropathies
  - Diabetes mellitus
  - Porphyria
  - Demyelinating disease
  - Other
- Cerebellar and midbrain disease
  - Multiple sclerosis
  - Trauma
  - Tumor
  - Other
- Idiopathic dystonia, including focal dystonia
- Psychogenic
- Drugs

tremor; however, 10% never have a tremor.[9] The classic tremor is a resting one, but a postural tremor that is similar to essential tremor can occur and may respond to the use of β-adrenergic blockers. The resting tremor consists of adduction-abduction of the fingers and hands. Flexion-extension of fingers in coordination with adduction-abduction of the thumb gives the classic "pill rolling" tremor. Resting tremor can affect also the legs, jaw, and lips. The frequency is 4 to 6 Hz, and the tremor occurs mainly distally. It dampens when hands are in motion and is asymmetrical at least initially. Emotional stress in particular increases the amplitude. The mainstay of the treatment of Parkinson's disease is a combination of carbidopa and levodopa. The effect on the tremor is variable, and some people may have a poor response. Anticholinergics such as trihexyphenidyl hydrochloride and benztropine mesylate can be useful, but are poorly tolerated especially by older patients.[9,12] Propranolol can be used as adjuvant treatment in doses similar to those used for essential tremor. Stereotactic thalamotomy or high-frequency stimulation of the thalamus directed to the nucleus ventralis intermedius should be considered.

Tremor With Other Basal Ganglia Diseases

Tremor can be a component of the symptom complex in patients with dystonic disorders, such as spasmodic torticollis.[5] The administration of botulinum toxin is effective for focal dystonia. Treatment of the underlying condition may also ameliorate the tremor. In Wilson's disease, tremor can be the presenting symptom. It can occur with postural and kinetic movements and is most prominent in the proximal muscles. At the shoulders it is described as "wing-beating" tremor. The treatment of Wilson's disease with penicillamine may ameliorate the tremor.[2]

Cerebellar Tremor

Patients with cerebellar disease have both postural and kinetic tremors. Various types of postural tremors have been described. The most common consist of oscillations of the arms about the shoulders or of the legs about the hips.[2] It is referred to as titubation when it affects the trunk and head. There is also a mild postural tremor that is more rapid (frequency of 10 Hz) with distal predominance. The characteristic cerebellar kinetic tremor has a frequency of 3 to 5 Hz. It is evident on finger-to-nose and heel-to-shin tests. It appears at the initiation and along the course of a movement and has a coarse side-to-side component. The amplitude of the tremor increases as the limb is extended or on approaching a target. The most common cause of cerebellar tremors is multiple sclerosis, but brain-stem tumors or strokes and degenerative and paraneoplastic diseases can also be responsible. Cerebellar tremors are thought to be due to lesions of the lateral cerebellar nuclei or superior cerebellar peduncle. Lesions of the midbrain around the red nucleus will produce a wing-beating type of tremor. Midline cerebellar disease (lesions in the vermis) will cause bilateral arm tremor and, more commonly, head and trunk tremor (titubation). No effective treatment exists for cerebellar tremors.

Tremor With Peripheral Neuropathy

Tremor is a rare manifestation of peripheral neuropathy. It is observed in some patients with idiopathic, demyelinating, hereditary motor and sensory and immunoglobulin M paraproteinemic neuropathies, and, less often, diabetes mellitus, uremia, diseases of anterior horn cells, and porphyria.[1] The tremor is similar clinically to essential tremor. Symptomatic treatment with propranolol, primidone, benzodiazepines, or baclofen is worth attempting. Treatment should be focused on the underlying neuropathy.

Posttraumatic Tremor

Tremor is well known as a consequence of head trauma and appears within a few months after the injury. The frequency is 4 to 6 Hz. It is typically proximal and made worse with movement.[13,14] These tremors may respond to the use of propranolol or stereotactic thalamotomy.[15]

Alcohol Withdrawal Tremor

Tremor is a symptom of alcohol withdrawal. It may occur after a period of relative or absolute abstinence. The earliest and most common withdrawal symptom is a generalized tremor, which has the characteristic of an enhanced physiologic tremor.[16] A more permanent postural tremor can sometimes occur in persons with chronic alcoholism even with alcohol abstinence.

Psychogenic Tremor

Tremor can be a manifestation of hysteria and occurs in young and old people alike. A patient commonly presents with complex tremors (combination of resting, pos-

tural, and kinetic). The history reveals an unusual temporal profile (abrupt onset with variable course), an absence of other neurologic symptoms, selective disability with the ability to perform some functions in the presence of severe tremor, and unusual handwriting. Some patients have a psychiatric history of multiple undiagnosed somatizations. If the affected limb is restrained, the tremor may move to another body part. Diagnosis is difficult, but an important clue is that it disappears when the patient's attention is distracted. Treatment of the underlying psychiatric problem may result in a disappearance of the tremor, but the prognosis is often poor.

Conclusion

Evaluating tremors can be straightforward and challenging at the same time. It is helpful to know if the tremor occurs at rest, with movement, or with a specific task. A history of tremors or movement disorder in the family and pharmacologic exposure can be important. Treatment is available but complicated by drug intolerance and a variable response.

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